

Appl. No. 10/719,429

Amdt. dated January 10, 2005

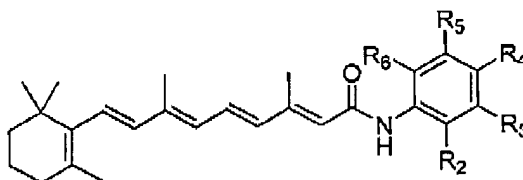
Reply to Notice of Non-Compliant Amendment of December 10, 2004

**Amendments to the Claims:**

This listing of claims will replace all prior versions, and listings, of claims in the application:

Claims 1 – 4 (canceled)

Claim 5. (currently amended) An arylretinamide for inducing apoptosis in a cancer cell, said arylretinamide having Structure A, B, or C below:



**Structure A**

wherein

R<sub>2</sub> is H, OH, NO<sub>2</sub>, CH<sub>2</sub> OH, a halide, or an alkyl comprising 1-4 carbon atoms,

R<sub>3</sub> is H, OH, NO<sub>2</sub>, CO<sub>2</sub>CH<sub>3</sub>, CO<sub>2</sub>CH<sub>2</sub>CH<sub>3</sub>, CO<sub>2</sub>(CH<sub>2</sub>)<sub>2</sub>CH<sub>3</sub>, CO<sub>2</sub>(CH<sub>2</sub>)<sub>3</sub>CH<sub>3</sub>, CO<sub>2</sub>H, CH<sub>2</sub>OH, a halide, or an alkyl comprising 1-4 carbon atoms;

R<sub>4</sub> is H, OH, OCH<sub>3</sub>, OCH<sub>2</sub>CH<sub>3</sub>, O(CH<sub>2</sub>)<sub>2</sub>CH<sub>3</sub>, O(CH<sub>2</sub>)<sub>3</sub>CH<sub>3</sub>, SO<sub>2</sub>CH<sub>3</sub>, SO<sub>2</sub>CH<sub>2</sub>CH<sub>3</sub>, SO<sub>2</sub>(CH<sub>2</sub>)<sub>2</sub>CH<sub>3</sub>, SO<sub>2</sub>(CH<sub>2</sub>)<sub>3</sub>CH<sub>3</sub>, NH<sub>2</sub>, NHCOCH<sub>3</sub>, NHCOCH<sub>2</sub>CH<sub>3</sub>, NHCO(CH<sub>2</sub>)<sub>2</sub>CH<sub>3</sub>, NHCO(CH<sub>2</sub>)<sub>3</sub>CH<sub>3</sub>, NHCOCF<sub>3</sub>, N<sub>3</sub>, NCS, NO<sub>2</sub>, a halide, an alkyl comprising 1-4 carbon atoms, or NHCOCX, wherein X is a halide;

R<sub>5</sub> is H, NO<sub>2</sub>, C(CH<sub>3</sub>)<sub>3</sub>, C(CH<sub>2</sub>CH<sub>3</sub>)<sub>3</sub>, C((CH<sub>2</sub>)<sub>2</sub>CH<sub>3</sub>)<sub>3</sub>, C((CH<sub>2</sub>)<sub>3</sub>CH<sub>3</sub>)<sub>3</sub>, CO<sub>2</sub>CH<sub>3</sub>, CO<sub>2</sub>CH<sub>2</sub>CH<sub>3</sub>, CO<sub>2</sub>(CH<sub>2</sub>)<sub>2</sub>CH<sub>3</sub>, CO<sub>2</sub>(CH<sub>2</sub>)<sub>3</sub>CH<sub>3</sub>, a halide, or an alkyl comprising 1-4 carbon atoms, and

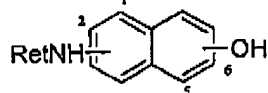
R<sub>6</sub> is H, CO<sub>2</sub>H, CO<sub>2</sub>CH<sub>3</sub>, CO<sub>2</sub>CH<sub>2</sub>CH<sub>3</sub>, CO<sub>2</sub>(CH<sub>2</sub>)<sub>2</sub>CH<sub>3</sub>, CO<sub>2</sub>(CH<sub>2</sub>)<sub>3</sub>CH<sub>3</sub>, a halide or an alkyl comprising 1-4 carbon atoms;

provided however that when R<sub>2</sub>, R<sub>3</sub>, R<sub>4</sub>, R<sub>5</sub>, and R<sub>6</sub> are all H, R<sub>4</sub> is not OH or OCH<sub>2</sub>CH<sub>3</sub>; and also provided that when R<sub>3</sub>, R<sub>5</sub>, and R<sub>6</sub> are all H, and R<sub>2</sub> is OH, R<sub>4</sub> is not CO<sub>2</sub>CH<sub>3</sub>.

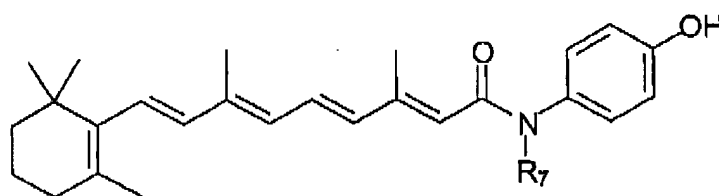
Appl. No. 10/719,429

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**Structure B**

wherein the OH group is at position 2,4, or 5 when the retinamido group is at linked to position 1, and the OH group is at position 3 when the retinamido group is linked to position 2.

**Structure C**

wherein R<sub>7</sub> is C<sub>1</sub> to C<sub>4</sub> alkyl.

Claim 6. (original) The arylretinamide of claim 5 wherein the arylretinamide is a halohydroxyphenyl retinamides which comprises a phenyl moiety that is optionally substituted with an alkyl group .

Claim 7. (original) The arylretinamide of claim 6 wherein the phenyl moiety is substituted with a methyl group.

Claim 8. (original) The arylretinamide of claim 6 wherein the halo group is an iodo group.

Claim 9. (original) The arylretinamide of claim 5 wherein the arylretinamide is a hydroxy-alkylphenyl retinamides or hydroxy-alkoxyphenyl retinamide, wherein the alkyl groups attached to the phenyl moiety comprise from 1 to 4 carbon atoms.

Claim 10. (original) The arylretinamide of claim 9 wherein the arylretinamide is a hydroxy-methylphenyl or hydroxy-methoxyphenyl retinamide.

Appl. No. 10/719,429

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Claim 11. (original) The arylretinamide of claim 5 is a hydroxy-nitrophenyl retinamides or alkylsulfonyl-hydroxy retinamides.

Claim 12. (original) The arylretinamide of claim 11 wherein the arylretinamide is an ethylsulfonyl-hydroxy, retinamides.

Claim 13. (original) The arylretinamide of claim 5 wherein the arylretinamide is a hydroxy-naphthylphenyl retinamide.

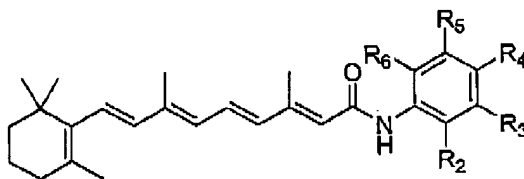
Claim 14. (original) The arylretinamide of claim 5 wherein the arylretinamide is an N-alkyl(hydroxyphenyl) retinamides.

Claim 15. (original) The arylretinamide of claim 5 wherein the arylretinamide is an aminophenyl retinamides.

Claim 16. (original) The arylretinamide of claim 5 wherein the arylretinamide is an alkylhydroxyphenyl retinamides.

Claim 17. (original) The arylretinamide of claim 5 wherein the arylretinamide is a carboxy-hydroxyphenyl retinamides selected from the group consisting of *N*-(2'-hydroxy-3'-carboxymethylphenyl)retinamide, *N*-(2'-hydroxy-3'-carboxyphenyl)retinamide, *N*-(2'-hydroxy-6'-carboxymethylphenyl)retinamide, *N*-(2'-hydroxy-6'-carboxyphenyl)retinamide, *N*-(3'-hydroxy-4'-carboxymethylphenyl)retinamide, *N*-(3'-hydroxy-4'-carboxyphenyl)retinamide, *N*-(2'-hydroxy-5'-carboxymethylphenyl)retinamide, *N*-(2'-hydroxy-4'-carboxyphenyl)retinamide, *N*-(4'-hydroxy-3'-carboxymethylphenyl)retinamide, and *N*-(4'-hydroxy-3'-carboxyphenyl)retinamide.

Claim 18. (currently amended) An arylretinamide having Structure A below



Structure A

Appl. No. 10/719,429

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wherein

$R_2$  is H, OH,  $\text{NO}_2$ ,  $\text{CH}_2\text{OH}$ , a halide, or an alkyl comprising 1-4 carbon atoms,

$R_3$  is H, OH,  $\text{NO}_2$ ,  $\text{CO}_2\text{CH}_3$ ,  $\text{CO}_2\text{CH}_2\text{CH}_3$ ,  $\text{CO}_2(\text{CH}_2)_2\text{CH}_3$ ,  $\text{CO}_2(\text{CH}_2)_3\text{CH}_3$ ,  $\text{CO}_2\text{H}$ ,  $\text{CH}_2\text{OH}$ , a halide, or an alkyl comprising 1-4 carbon atoms;

$R_4$  is H, OH,  $\text{OCH}_3$ ,  $\text{OCH}_2\text{CH}_3$ ,  $\text{O}(\text{CH}_2)_2\text{CH}_3$ ,  $\text{O}(\text{CH}_2)_3\text{CH}_3$ ,  $\text{SO}_2\text{CH}_3$ ,  $\text{SO}_2\text{CH}_2\text{CH}_3$ ,  $\text{SO}_2(\text{CH}_2)_2\text{CH}_3$ ,  $\text{SO}_2(\text{CH}_2)_3\text{CH}_3$ ,  $\text{NH}_2$ ,  $\text{NHCOCH}_3$ ,  $\text{NHCOCH}_2\text{CH}_3$ ,  $\text{NHCO}(\text{CH}_2)_2\text{CH}_3$ ,  $\text{NHCO}(\text{CH}_2)_3\text{CH}_3$ ,  $\text{NHCOCF}_3$ ,  $\text{N}_3$ ,  $\text{NCS}$ ,  $\text{NO}_2$ , a halide, an alkyl comprising 1-4 carbon atoms, or  $\text{NHCOCH}_2\text{X}$ , wherein X is a halide;

$R_5$  is H,  $\text{NO}_2$ ,  $\text{C}(\text{CH}_3)_3$ ,  $\text{C}(\text{CH}_2\text{CH}_3)_3$ ,  $\text{C}((\text{CH}_2)_2\text{CH}_3)_3$ ,  $\text{C}((\text{CH}_2)_3\text{CH}_3)_3$ ,  $\text{CO}_2\text{CH}_3$ ,  $\text{CO}_2\text{CH}_2\text{CH}_3$ ,  $\text{CO}_2(\text{CH}_2)_2\text{CH}_3$ ,  $\text{CO}_2(\text{CH}_2)_3\text{CH}_3$ , a halide, or an alkyl comprising 1-4 carbon atoms, and

$R_6$  is H,  $\text{CO}_2\text{H}$ ,  $\text{CO}_2\text{CH}_3$ ,  $\text{CO}_2\text{CH}_2\text{CH}_3$ ,  $\text{CO}_2(\text{CH}_2)_2\text{CH}_3$ ,  $\text{CO}_2(\text{CH}_2)_3\text{CH}_3$ , a halide, or an alkyl comprising 1-4 carbon atoms;

provided that when  $R_2$ ,  $R_3$ ,  $R_4$ ,  $R_5$ , and  $R_6$  are all H,  $R_4$  is not OH,  $\text{OCH}_3$ ,  $\text{OCH}_2\text{CH}_3$ , or  $\text{O}(\text{CH}_2)_2\text{CH}_3$ ; and also

provided that when  $R_3$ ,  $R_5$ , and  $R_6$  are all H, and  $R_2$  is OH,  $R_4$  is not  $\text{CO}_2\text{CH}_3$  or  $\text{CO}_2\text{CH}_2\text{CH}_3$ .

Claim 19. (original) A method of inducing apoptosis in a cancer cell comprising contacting the cancer cell with an arylretinamide of claim 1.

Claim 20. (original) A method of treating cancer in a subject in need of said treatment, comprising administering one or more arylretinamides of claim 1 to the subject.

Claim 21. (original) The method of claim 20 wherein said method further comprises administering calcium glucarate to the subject.